http://jppbr.ub.ac.id/
DOI: 10.21776/ub.jppbr.2023.004.02.3
eISSN: 2723-083X pISSN: 2723-0821

Journal of Psychiatry Psychology and Behavioral Research
Vol. 4, No. 2, September 2023

JPPBR

DRESS SYNDROME AS SERIOUS SKIN HYPERSENSITIVITY REACTIONS ASSOCIATED WITH OLANZAPINE: CASE REPORT

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CASE REPORT **OPEN ACCESS**

ABSTRACT

Introduction – There are a variety of symptoms associated with this serious idiosyncratic adverse reaction, including fever, skin eruption, lymphadenopathy, eosinophilia, organ involvement, and hematologic abnormalities which clinical manifestations occur two weeks to two months after a triggering drug was administrated.
Methods – Presented the case of a 50-year-old male who developed severe generalized erythroderma with exfoliative scaling skin erythema and maculopapular eruptions all over the body. This was associated with fever, eosinophilia, and leukocytosis after olanzapine ingestion.
Results – This case called Dress syndrome, and the atypical antipsychotic olanzapine is one of the causes of this illness. This adverse effect is life-threatening, so early diagnosis reduces morbidity and mortality.
Discuss – It is imperative that health care professionals and caregivers are aware of the symptoms of such life-threatening reactions during and after treatment. It is also necessary to understand the pathogenesis of diseases in order to develop personalized treatment plans. The medication history of patients with suspected DRESS must be checked.
Conclusion – Dress syndrome is a serious and potentially devastating side effect of psychotropic medication. It is possible to experience adverse drug reactions after one dose or prolonged use of a drug or following a combination of two or more drugs. It is important for health care professionals and caregivers to be aware of the symptoms of such life -threatening reactions as part of the aftercare process during treatment. In order to develop personalized treatment plans, more research is necessary to elucidate its pathogenesis. It is imperative to check the medication history of patients with suspected DRESS. Usually, a patient who has previously taken a suspected drug will experience symptoms within two weeks of taking it.

Keywords: Olanzapine, psychosis, drug hypersensitivity syndrome, skin rash.

Article History:
Received: July 29, 2023
Accepted: August 16, 2023
Published: September 30, 2023

Cite this as: *Siddiqui, J.A., Qureshi, S.F., Hafez, A.A., Marei, W.M Dress Syndrome as Serious Skin Hypersensitivity Reactions associated with Olanzapine: a Case Report. Journal of Psychiatry Psychology and Behavioral Research; 2023.4(2):10-13.*

INTRODUCTION

DRESS syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms) is a serious adverse hypersensitivity reaction also called drug hypersensitivity syndrome. There are a variety of symptoms associated with this serious idiosyncratic adverse reaction, including fever, skin eruption, lymphadenopathy, eosinophilia, organ involvement, and hematologic abnormalities.[1] In most cases, clinical manifestations occur two weeks to two months after a triggering drug has been administered.[2,3] Drug-induced hypersensitivity syndromes (DIHS) are used in Japan,[4] while drug reactions with eosinophilia and systemic symptoms (DRESS) are used in other countries.[5] An atypical antipsychotic drug like olanzapine can cause serious adverse drug reactions and idiosyncratic reactions that need hospitalization and can lead to life-threatening complications if not treated promptly.[6] The number of people who develop Olanzapine-induced dress syndrome is 1 in 1000 to 10,000. It is associated with significant morbidity and mortality, and ten percent of cases succumb to it. In order to prevent future occurrences, it is imperative to manage the condition with an accurate diagnosis and prompt treatment.

In psychiatry, olanzapine is frequently prescribed, causing this rare, fatal, and life-threatening side effect. A new warning is being added to all olanzapine-containing drug labels by the United States Food and Drug Administration.[7] There are two fundamental pathophysiological factors causing dress that are

inciting stimuli, such as drugs and viruses. Firstly, drugs such as anticonvulsants like carbamazepine, lamotrigine, phenobarbital and phenytoin sodium; antibiotics like minocycline, vancomycin and sulfasalazine; psychotropic drugs like amitriptyline, clomipramine, mirtazapine, bupropion, benzodiazepines and olanzapine; and other drugs like allopurinol, dapsone. Secondly, viruses such as human herpes virus (HHV), HHV-6 is the most frequent HHV associated with DRESS, and its reactivation typically occurs during DRESS and up to 2–3 weeks, other viruses like epstein–Barr virus (EBV), and cytomegalovirus (CMV) that can undergo reactivation.[8-10] Dress syndrome has an unknown pathogenesis. Despite the fact that the pathogenic process is still unclear, the following mechanisms have been suggested: (a) immunological hypersensitivity reactions (type IV), with genetic vulnerability determined by HLA types. HLA-restricted aberrant T-cell activation; (b) viral reactivation (particularly HHV-6); and (c) expansion of regulatory T-cells. It typically occurs 2–6 weeks after drug intake, followed by (d) eosinophilic inflammation.[11]There are a variety of conditions that can mimic DRESS syndrome, such as viral or bacterial infections, connective tissue conditions, Still's disease, and hematological disorders. There are no known genetic susceptibility factors for this disease.

METHOD

Presented the case of a 50-year-old male who developed severe generalized erythroderma with exfoliative scaling skin erythema and maculopapular eruptions all over the body. This was associated with fever, eosinophilia, and leukocytosis after olanzapine ingestion.

This study was approved by the Ethical Committee of Research and Studies Department, Directorate of Health Affairs, Taif, Saudi Arabia. IRB Registration Number with KACST, KSA: HAP-02-T-067, approval number: 832.

Figure 1. Shows hand swelling, discharge of yellowish fluid with scales associated with morbilliform rash.

CASE REPORT

A 50-year-old man with a known case of schizophrenia for 25 years. He was admitted to our hospital by the Red Crescent ambulance authority along with a family member with a one-month history of disturbed behavior such as muttering to himself, hearing voices, and threatening his family with a knife. On mental state examination, he was restless, neglected himself, angry, and agitated. His mood was irritable, with a restricted effect. There is no evident delusion, but auditory hallucinations are present with poor attention and concentration. He has a history of amphetamine abuse but has abstained from the drug for four years. The results of all other relevant investigations, such as a complete blood count, serum electrolytes, and kidney and liver function tests, were all normal. He was taking risperidone 2 mg twice daily, but he did not improve, so the treating team slowly tapered his medications and started olanzapine 5 mg once daily, gradually increasing to 10 mg. The patient showed improvement after two weeks of taking the medications. Later, the patient developed a fever, which rose to 38.5°C on day 14 of taking olanzapine and persisted for 4 days. We observed hand swelling and discharge of yellowish fluid with scales associated with morbilliform rash, depicted in Figure 1. Figure 2 shows redness and swelling on both legs with rashes. Figure 3 shows a generalized erythroderma rash with swelling and exfoliative scaling on both hands. He had a high leukocyte count ($20.20X10^3$/uL) and a raised eosinophil count (24.5%) in addition to a high leukocyte count. There were no significant changes detected on his electrocardiogram (ECG) or chest X-ray. An ultrasound (USG) of his whole abdomen revealed 110 ml of peritoneal fluid. The patient was immediately referred to a dermatologist.

Figure 2. Shows redness and swelling on both legs with rashes.

Figure 3. Shows a generalized erythroderma rash with swelling and exfoliative scaling on both hands.

RESULT

Report by the dermatologist concluded that this was a case of olanzapine-induced Dress syndrome after taking a detailed medical history. It was suspected that the rashes were caused by a drug eruption, and olanzapine was discontinued. The patient was started on a systemic corticosteroid (methyl prednisolone 60 mg intramuscularly given twice a day), an antihistaminic agent (cetirizine 10 mg per day), a topical steroid (clobetasol lotion), and an antipyretic (paracetamol 1000 mg twice daily for 5 days). Initially, the skin lesions worsened after discontinuation of olanzapine but improved after steroids were administered. Even though the skin eruption improved on day 20, his fever gradually decreased, and he gradually improved symptomatically. His blood test results returned to baseline after one month, and his skin rash subsided. After 30 days of dermatological treatment, we observed a complete recovery. The patient was discharged on oral haloperidol 5 mg per day. We inform the patient and the caretakers of any red-flag signs of possible adverse reactions. He is currently taking 5 mg of haloperidol orally. His biological functions are normal, and he is free of psychotic symptoms. It has not been reported that haloperidol causes any particular adverse reactions, especially extrapyramidal side effects.

DISCUSS

In our case, the typical skin rash and fever are thought to be due to Dress syndrome caused by olanzapine. This case raises notable points regarding the rapid onset of illness that occurred only after two weeks of starting olanzapine. As the medication history is unclear, the rapid onset of illness might be due to previous sensitization to olanzapine prior to hospitalization. Since no other drugs were administered at the time of the rash, Additionally, Olanzapine was considered the most offending agent in this case. This is because of the clear temporal association of Olanzapine introduction with the development of Dress syndrome symptoms, which is followed by improvement of the symptoms after its withdrawal.

In our case pathophysiological pillars causing dress syndrome are culprit drug olanzapine. It causes immunological hypersensitivity reactions (type IV), leads to morbilliform rashes all over the body and another causative factor could be reactivation of the virus. The immune system is believed to play a key role in trigger drug action from a pathophysiological perspective. Additionally, culprit drugs may also play a role in viral reactivation as well as deranged immune responses. Early manifestations of DRESS may be caused by viruses causing direct tissue damage. A final point to consider is the relationship between eosinophil activation and multiplication and the immune response to culprit drugs that lead to organ eosinophil infiltration. We found that a single drug was the etiological agent in our case. After we identify that there is a single drug responsible for these symptoms, the notorious agent must be stopped, as part of management. Additionally, corticosteroids should be used judiciously, and supportive care must be provided.[12, 13] There were management challenges in this case. Therefore, there are limited antipsychotic choices for managing this case. Haloperidol was finally chosen for this patient since risperidone failed to provide improvement in this case.

In Dress syndrome, the morbilliform rash is the most commonly seen cutaneous manifestation. It is characterized by diffuse, pruritic, macular, and occasionally erythematous exanthema. There is a classic cutaneous distribution that involves the face, upper trunk, and upper and lower extremities, but it may also involve the entire surface of the skin. In Dress syndrome, the liver is the most frequently affected visceral organ and is often associated with hepatitis and eosinophilia. A similar clinical picture was shown in our patient, who developed a diffuse, pruritic, morbilliform, and erythematous rash. This was associated with fever, hepatitis, and eosinophilia.

CONCLUSION

Dress syndrome is a serious and potentially devastating side effect of psychotropic medication. It is possible to experience adverse drug reactions after one dose or prolonged use of a drug or following a combination of two or more drugs. It is important for health care professionals and caregivers to be aware of the symptoms of such life -threatening reactions as part of the aftercare process during treatment. In order to develop personalized treatment plans, more research is necessary to elucidate its pathogenesis. It is imperative to check the medication history of patients with suspected DRESS. Usually, a patient who has previously taken a suspected drug will experience symptoms within two weeks of taking it.

Conflicts of interest: the authors declared there was no conflict of interest.

Author contributions: JAS- material preparation, conception and design, or acquisition of data, or analysis and interpretation of data, SFQ- draft of the manuscript was written, drafting or revising it critically for significant intellectual content. AAH & WMM- Critical review and editing of the final manuscript was done.

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